# ADDENDUM

**Review and Evaluation of Clinical Data**
**NDA #021436/027**

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| **Sponsor:** | Otsuka Pharmaceutical Co, Ltd |
| **Drug:** | Aropiprazole |
| **Proposed Indication:** | Irritability Associated with Autistic Disorde |
| **Material Submitted:** | Original sNDA submission |
| **Correspondence Date:** | 21 January 2009 |
| **Date Received:** | 22 January 2009 |
| **Related NDA:** | |

This sNDA was submitted on 21 January 2009 and my original clinical review was completed on 30 October 2009 and has been filed into DARRTS. Due to technical problems that occured while the Word file (my review) was converted to a PDF file, part of the information (track-changes) in section of 9.2 Labeling Recommendations was lost in DARRTS. This addendum includes the original review of section 9.2 Labeling Recommendations.

## 9.2 Labeling Recommendations

The following are the sponsor proposed changes and the reviewer's recommendations. Changes are shown as ~~strikethroughs~~ for deletion and underline for addition.

In section 6.1 Overall Adverse Reactions Profile/Weight Gain, the sponsor proposed following addition:

(b) (4)

In section 14.4, the sponsor proposed following addition:

*14.4 Irritability Associated with Autistic Disorder*

*Pediatric Patients*

*The efficacy of ABILIFY (aripiprazole) in the treatment of irritability associated with Autistic Disorder was established in two 8-week, placebo-controlled trials in*

*pediatric patients (6 to 17 years of age) who met the DSM-IV criteria for Autistic Disorder and demonstrated behaviors such as tantrums, aggression, self-injurious behavior, or a combination of these problems. Over 75% of these subjects were under 13 years of age.*

*Efficacy was evaluated using two assessment scales: the Aberrant Behavior Checklist (ABC) and the Clinical Global Impression-Improvement (CGI-I) scale. The primary outcome measure in both trials was the change from baseline to endpoint in the Irritability subscale of the ABC (ABC-I). The ABC-I subscale measured the emotional and behavioral symptoms of irritability in Autistic Disorder, including aggression towards others, deliberate self-injuriousness, temper tantrums, and quickly changing moods.* (b) (4)

*The results of these trials are as follows:*

*1. In one of the 8-week, placebo-controlled trials, children and adolescents with Autistic Disorder (n=98), aged 6 to 17 years, received daily doses of placebo or ABILIFY 2 mg/day to 15 mg/day. ABILIFY, starting at 2 mg/day* (b) (4) *up to 15 mg/d base on clinical response* (b) (4) *significantly improved scores on the ABC-I subscale and on the CGI-I scale compared with placebo. The mean daily dose of aripiprazole at the end of 8 weeks was 8.6 mg/day.*

*2. In the other 8-week, placebo-controlled trial in children and adolescents with Autistic Disorder (n=218), aged 6 to 17 years, three fixed doses of ABILIFY (5 mg/day, 10 mg/day, or 15 mg/day) were compared to placebo. ABILIFY dosing started at 2 mg/day and was increased to 5 mg/day after one week. After a second week, it was increased to 10 mg/day for patients in the 10 mg and 15 mg dose arms, and after a third week, it was increased to 15 mg/day in the 15 mg/day treatment arm. All three doses of ABILIFY significantly improved scores on the ABC-I subscale compared with placebo.*

The reviewer has reviewed all other proposed clinical related labeling changes. The rest proposed changes are acceptable.

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November 1, 2009

cc: NDA 21436/027
HFD-130 (Div. File)
HFD-130 /T Laughren
/M Mathis
/R Temple
/J Zhang
/K Ansah

| Application Type/Number | Submission Type/Number | Submitter Name | Product Name |
|---|---|---|---|
| NDA-21436 | SUPPL-27 | OTSUKA PHARMACEUTICAL CO LTD | ABILIFY (ARIPIPRAZOLE) 10/15/20/30MG |

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/s/

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JING ZHANG
11/01/2009